

AMBERLITE IR-120 RESIN MEDIATED RAPID SYNTHESIS OF QUINOXALINES

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ABSTRACT

A simple and convenient synthesis of quinoxalines by the reaction of substituted phenacyl bromides with o-phenylene diamines using Amberlite IR-120 resin as a reusable catalyst. This method is a simple, mild, recyclable catalyst and practically easy workup. The catalyst can be easily separated from the reaction by simple filtration and reused up to five catalytic cycles without major loss of catalytic activity.

KEYWORDS: Amberlite IR-120; Catalyst; Quinoxalines; Recyclability & Characterization

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INTRODUCTION

Quinoxalines are nitrogen comprising heterocyclic structures, which are having broad biological applications such as antibacterial,^[1] anticancer,^[2] antiviral,^[3] anti-HIV,^[4] kinase inhibition,^[5] etc. Many drugs are having quinoxaline ring as a structural core.^[6] Quinoxalines derivatives are having several applications in dyes,^[7] electroluminescent material,^[8] semiconductors,^[9] and chemical manageable switches.^[10] Further, due to the importance of quinoxalines there is an eco-friendly method is required to develop an ideal method for the synthesis of quinoxalines and their derivatives.

In the literature, numerous synthetic methods have been stated to constitute quinoxaline scaffold. The condensation of o-phenylenediamine with 1,2-dicarbonyl compounds,^[11-14] 1,2-diazenylbutens^[15] and oxidation trapping of α-hydroxy ketones^[16-18] are few of the reported synthetic methods. These synthetic methods have involved the presence of various catalysts such as citric acid,^[19] heteropoly acid,^[20] CSA,^[21] PEG-400,^[21] I₂ (III) in PEG-400,^[23] polyaniline-sulfate salt,^[24] CAN,^[18] MnO₂,^[18] fluorinated alcohols,^[25].

Among these few synthetic methods of quinoxalines, one of the methods the condensation of o-phenylenediamine with phenacyl bromides in the solid phase is highly preferred.^[25] This method has been reported by using catalyst-free approach,^[26] transition metal-catalyzed approaches^[27-29] as well as with various heterogeneous catalysts like HClO₄-SiO₂,^[30] TMSCl,^[31] β-cyclodextrin,^[32] micellar SDS,^[33] silica-supported phosphomolybdic acid,^[34] T3PDMSO or T3P,^[35] N-Bromosuccinimide^[36] and DABCO.^[37] Due to disadvantages in the present catalyst, there is a necessity to develop a new method using new catalysts having recyclability to be environmentally benign.

Usage of acidic resin in chemical reaction has gained importance in organic synthesis due to reusable, operational simplicity and chromatographic free. For this, we are interested to use, Amberlite-IR 120 resin as an efficient heterogeneous catalyst for chemical reactions^[38-39].

RESULTS AND DISCUSSIONS

To find the feasibility of the formation of quinoxalines, we tested a model reaction using *o*-phenylenediamine (**1a**) and phenacyl bromide (**2a**) using Amberlite IR-120 resin (10 mol%) as a catalyst in DMF as solvent at 60 °C for 30 min. The reaction was screened for its feasibility in different solvents. Among all the solvent reactions in DMF (Table-1) was giving the best yield. The reaction was optimal when 10% Amberlite IR-120 resin was used a catalyst. The optimal reaction conditions are phenacyl bromides (**2a**) (1 mmol) and *o*-phenylenediamines (**1a**) (1 mmol) using Amberlite IR-120 resin (10 mol%) as a catalyst in DMF as solvent at 60 °C for 30 min.

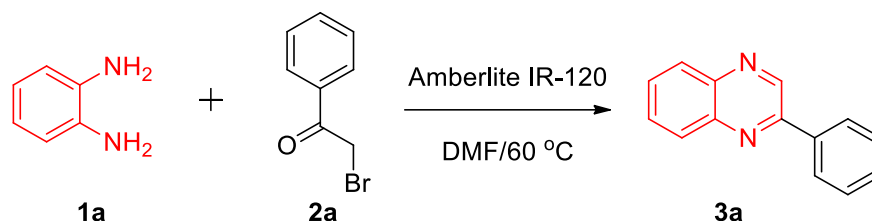


Table 1: Optimizing the Reaction Condition between *o*-Phenylenediamine and Phenacyl Bromide to get 3aa

S.No	Solvent	Catalyst	Yield ^b (%)
1	Water	Amberlite IR-120 (10 mol%)	NR
2	Methanol	Amberlite IR-120 (10 mol%)	58
3	Ethanol	Amberlite IR-120 (10 mol%)	62
4	Dichloromethane	Amberlite IR-120 (10 mol%)	65
5	Acetonitrile	Amberlite IR-120 (10 mol%)	72
6	DMF	Amberlite IR-120 (10 mol%)	98
7	DMF	Amberlite IR-120 (20 mol%)	97
8	DMF	Amberlite IR-120 (5 mol%)	82
9	DMF	No catalyst	14

Reaction conditions: Phenacyl bromide (1 mmol), *o*-phenylenediamine (1 mmol), 10% Amberlite IR-120 resin in 10 ml DMF, at 60 °C for 30 min. ^bIsolated yields.

NR: no reaction.

To understand the flexibility of the current method, different phenacyl bromides (**2a-m**) (1 mmol) and *o*-phenylenediamines (**1a-b**) (1 mmol) using Amberlite IR-120 resin (10 mol%) as a catalyst in DMF as solvent at 60 °C. All the reactions were going smoothly by forming the desired product in excellent yield without any purification. The structures of all the synthesized quinoxalines (**3a-s**) are shown in Figure 2. Optimization of the reaction parameters was performed by general model reaction of *o*-phenylenediamine (**1a**) and phenacyl bromide (**2a**) as shown below

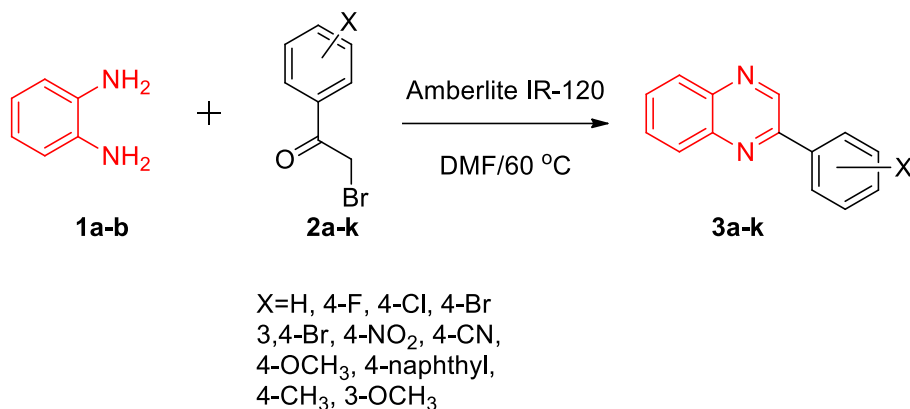


Figure 1: Preparation of Quinoxalines using Amberlite IR-120 Resin Catalyst.

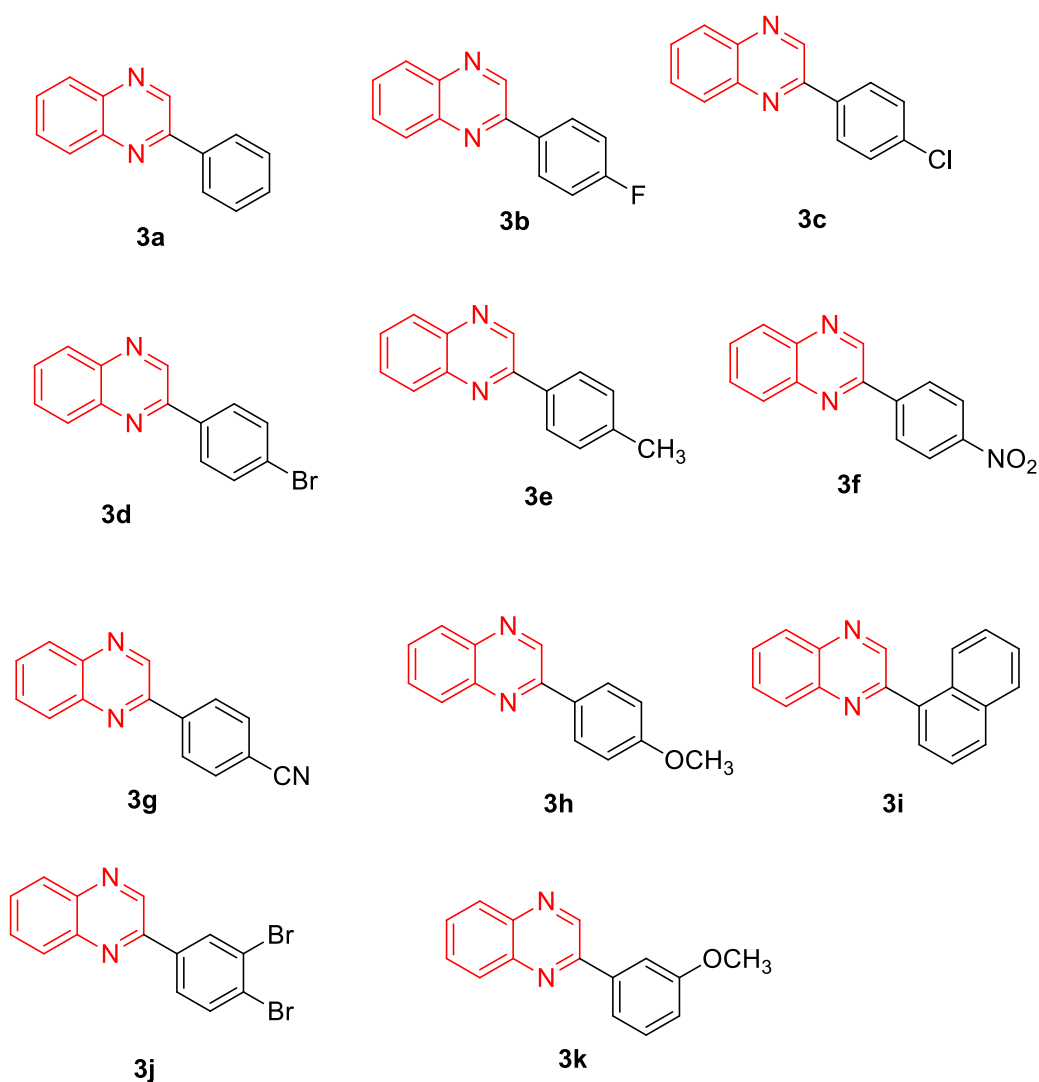


Figure 2: Structures of all the Synthesized Quinoxalines (3a–k).

These results invigorated the team to explore the possibility of the methodology for the preparation of quinoxalines using different phenacyl bromides and *o*-phenylenediamines in optimized reaction conditions using 10 mol% of Amberlite IR-120 catalyst and dimethylformamide (DMF) as solvent.

We have also investigated the recyclability of Amberlite IR-120 catalyst using model reaction between *o*-phenylenediamine (**1a**) and phenacyl bromide (**2a**) in DMF solvent at 60°C for 30 min and results were depicted in Table 2.

Amberlite IR-120 catalyst was recovered by filtration and recycled five times without losing any catalytic activity and the product isolated after the 4th recycle was much consistent in comparison with the fresh Amberlite IR-120 resin catalyst.

Experimental

Procedure for the Synthesis of Quinoxalines

A mixture of phenacyl bromide (1 mmol) and Amberlite IR-120 resin (10 mol%) was stirred in 10 ml DMF solvent at RT for 0.5 h. Then *o*-phenylenediamine (1 mmol) was added slowly and the resultant mixture was stirred for 10 min at RT and heated for another 0.5 h. After completion of the reaction, it was diluted with EtOAc (10 ml) and filtered to recover the catalyst. The filtrate was washed with aq NaHCO₃ and the organic layer was separated. After evaporation of the organic layer the crude product was obtained which on precipitation using ethanol afforded the pure quinoxaline.

Spectral Data of the Selected Compounds

- **2-Phenylquinoxaline (3a).** Yield 97%, pale yellow solid; IR (KBr, cm⁻¹): 3065, 1545, 1489, 1448, 1317, 1032; ¹H NMR (CDCl₃, 400 MHz): δ 9.38 (s, 1H), 8.08-8.16 (m, 4H), 7.79-7.86 (m, 2H), 7.56-7.64 (m, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ (ppm) 151.8, 143.3, 141.5, 136.7, 130.3, 130.2, 129.6, 129.5, 129.2, 129.1, 127.5.
- **2-(4-Chlorophenyl)quinoxaline (3c).** Yield 92%, yellow solid; IR (KBr, cm⁻¹): 3456, 3064, 1542, 1490, 1318, 1089; ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 9.31 (s, 1H), 8.14-8.17 (m, 4H), 7.75-7.83 (m, 2H), 7.55 (d, 2H); ¹³C NMR (CDCl₃, 100 MHz): δ (ppm) 150.6, 142.8, 142.4, 141.9, 136.8, 135.5, 130.6, 129.8, 129.9, 129.4, 129.7, 128.5.
- **2-(4-Bromophenyl)quinoxaline (3d).** Yield 94%, pale yellow solid; IR (KBr, cm⁻¹): 1590, 1542, 1486, 1126, 1078, 1048; ¹H NMR (CDCl₃, 400 MHz): δ 9.31 (s, 1H), 8.08-8.16 (m, 4H), 7.76-7.83 (m, 2H), 7.69 (d, 2H); ¹³C NMR (CDCl₃, 100 MHz): δ 151.2, 142.9, 142.5, 141.8, 136.5, 132.4, 130.7, 129.9, 129.6, 129.3, 128.3, 124.6;

CONCLUSIONS

In conclusion, we developed a mild, effective and environmentally caring synthetic method for the synthesis of quinoxalines (**3a-s**) from substituted phenacyl bromides and *o*-phenylenediamines using Amberlite IR-120 as a green and recyclable catalyst. The key feature of the protocol involves simple reaction conditions, no column purification, reusability of the catalyst.

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